

What is claimed is:

- 00023481-033004
1. A method for sequencing DNA by detecting the identity of a dideoxynucleotide incorporated to the 3' end of a DNA sequencing fragment using mass spectrometry, which comprises:
- (a) attaching a chemical moiety via a linker to a dideoxynucleotide to produce a labeled dideoxynucleotide;
  - (b) terminating a DNA sequencing reaction with the labeled dideoxynucleotide to generate a labeled DNA sequencing fragment, wherein the DNA sequencing fragment has a 3' end and the chemical moiety is attached via the linker to the 3' end of the DNA sequencing fragment;
  - (c) capturing the labeled DNA sequencing fragment on a surface coated with a compound that specifically interacts with the chemical moiety attached via the linker to the DNA sequencing fragment, thereby capturing the DNA sequencing fragment;
  - (d) washing the surface to remove any non-bound component;
  - (e) freeing the DNA sequencing fragment from the surface; and
  - (f) analyzing the DNA sequencing fragment using mass spectrometry so as to sequence the DNA.
2. A method for sequencing DNA by detecting the identity of a plurality of dideoxynucleotides incorporated to the 3' end of different DNA

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- (f) analyzing the DNA sequencing fragments using mass spectrometry so as to sequence the DNA.

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- SubBI

and the compound on the surface comprises a biotin-streptavidin interaction, a phenylboronic acid-salicylhydroxamic acid interaction, or an antigen-antibody interaction.

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- Sub B1
5. The method of claim 1 or 2, wherein the step of freeing the DNA sequencing fragment from the surface comprises disrupting the interaction between the chemical moiety attached via the linker to the DNA sequencing fragment and the compound on the surface.

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6. The method of claim 5, wherein the interaction is disrupted by a means selected from the group consisting of one or more of a physical means, a chemical means, a physical chemical means, heat, and light.

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7. The method of claim 1 or 2, wherein the dideoxynucleotide comprises a cytosine or a thymine with a 5-position, or an adenine or a guanine with a 7-position, and the linker is attached to the 5-position of cytosine or thymine or to the 7-position of adenine or guanine.

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8. The method of claim 1 or 2, wherein the step of freeing the DNA sequencing fragment from the surface comprises cleaving the linker.

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9. The method of claim 8, where the linker is cleaved by a means selected from the group consisting of one or more of a physical means, a

10. The method of claim 9, wherein the linker is cleaved by ultraviolet light.

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11. The method of claim 1 or 2, wherein the linker comprises a derivative of 4-aminomethyl benzoic acid.

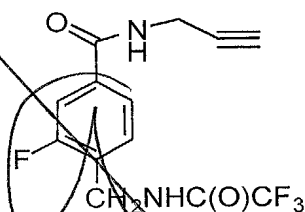
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12. The method of claim 11, wherein the linker comprises one or more fluorine atoms.

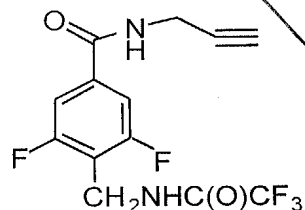
Sub B3

[illegible]

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Sub B4

16. The method of claim 1 or 2, wherein the chemical moiety comprises biotin, the labeled dideoxynucleotide is a biotinylated dideoxynucleotide, the labeled DNA sequencing fragment is a biotinylated DNA sequencing fragment, and the surface is a streptavidin-coated solid surface.

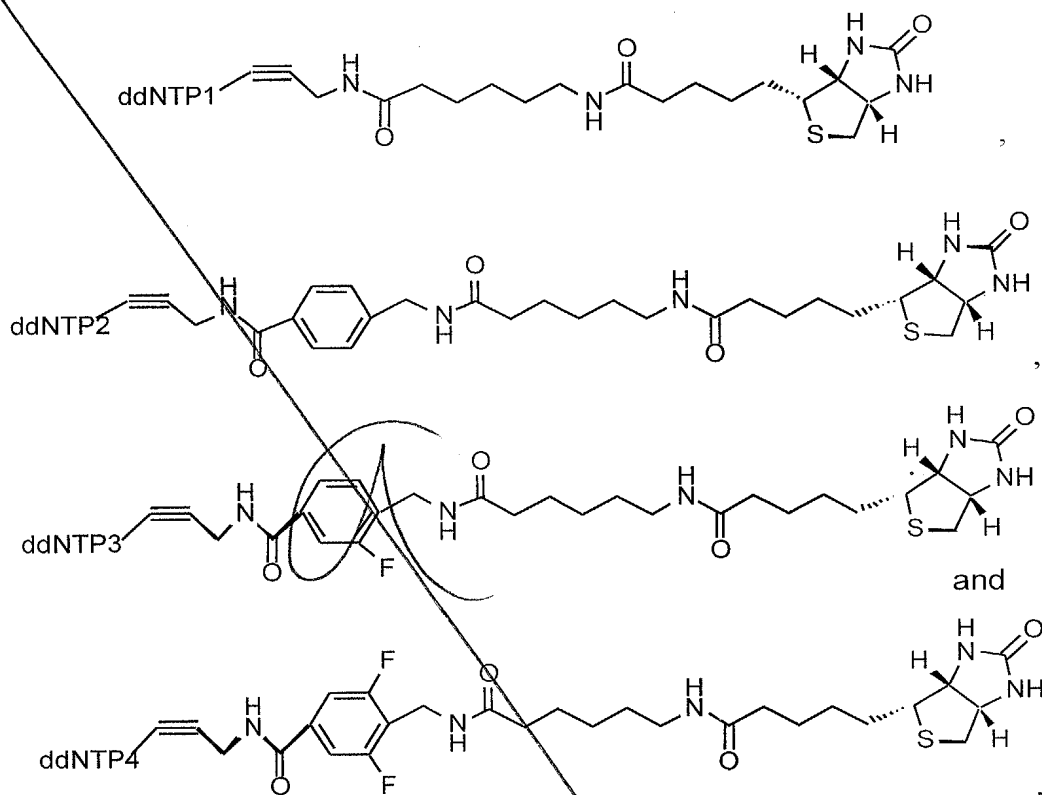
17. The method of claim 16, wherein the biotinylated dideoxynucleotide is selected from the group consisting of ddATP-11-biotin, ddCTP-11-biotin, ddGTP-11-biotin, and ddTTP-16-biotin.

Add B5

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18. The method of claim 16, wherein the biotinylated dideoxynucleotide is selected from the group consisting of:

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wherein ddNTP1, ddNTP2, ddNTP3, and ddNTP4 represent four different dideoxynucleotides.

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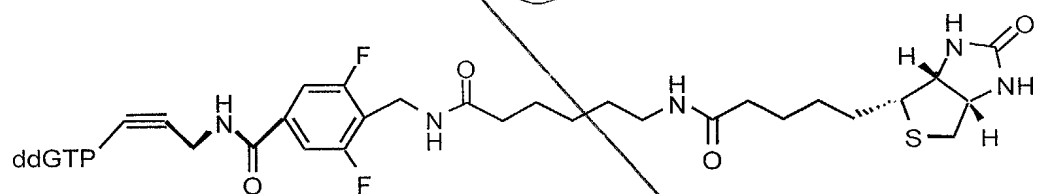
consisting of:

ddCTP

ddTTP

ddATP

ddGTP

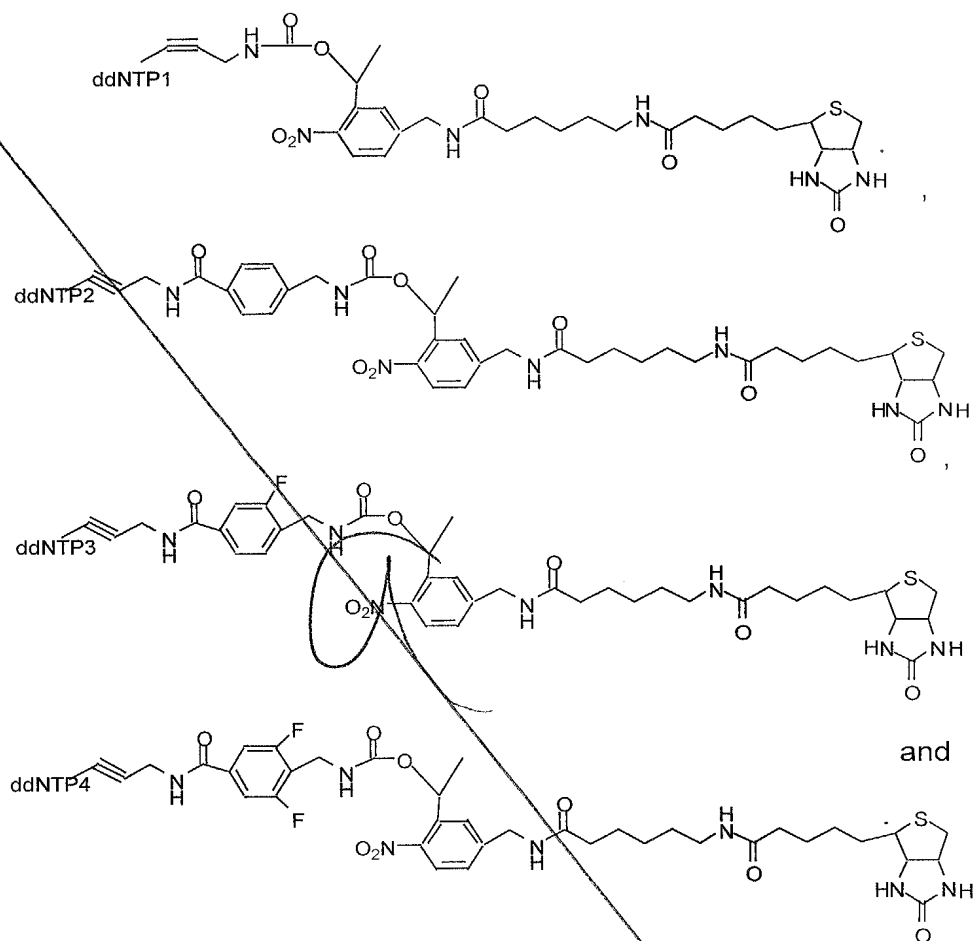


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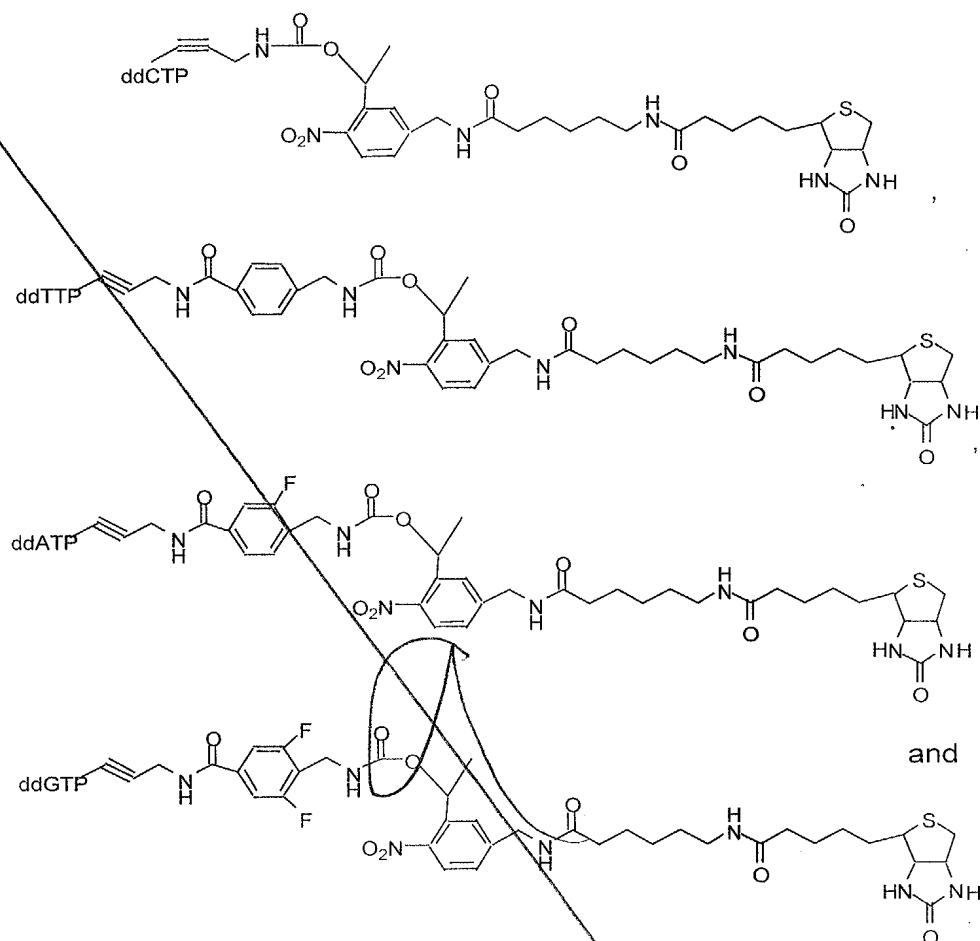
20. The method of claim 16, wherein the biotinylated dideoxynucleotide is selected from the group consisting of:

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wherein ddNTP1, ddNTP2, ddNTP3, and ddNTP4 represent four different dideoxynucleotides.

21. The method of claim 20, wherein the biotinylated dideoxynucleotide is selected from the group consisting of:



22. The method of claim 16, wherein the streptavidin-coated solid surface is a streptavidin-coated magnetic bead or a streptavidin-coated silica glass.

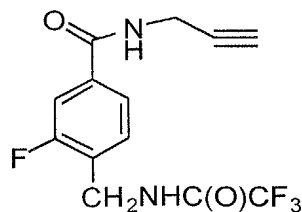
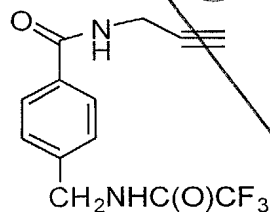
23. The method of claim 1 or 2, wherein steps (b) to (e) are performed in a single container or in a plurality of connected containers.

24. Use of the method of claim 1 or 2 for detection of single nucleotide polymorphisms, genetic mutation analysis, serial analysis of gene expression, gene expression analysis, identification in forensics, genetic disease association studies, genomic sequencing, translational analysis, or transcriptional analysis.

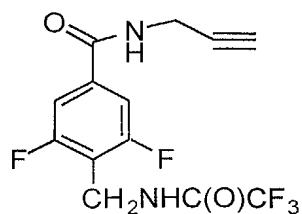
25. A linker for attaching a chemical moiety to a dideoxynucleotide, wherein the linker comprises a derivative of 4-aminomethyl benzoic acid.

26. The linker of claim 25, wherein the linker comprises one or more fluorine atoms.

27. The linker of claim 26, wherein the linker is selected from the group consisting of:



and



5      28. The linker of claim 25, wherein the linker is  
cleavable by a means selected from the group  
consisting of one or more of a physical means, a  
chemical means, a physical chemical means, heat,  
and light.

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cleavable by ultraviolet light.

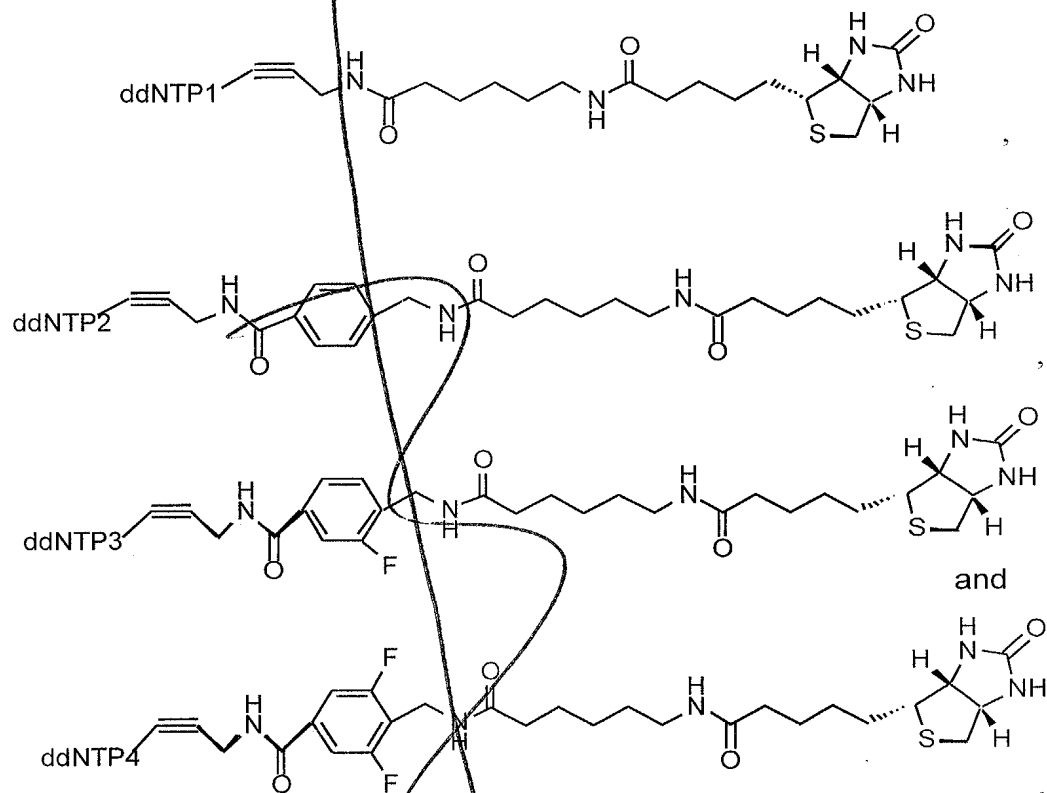
15      30. The linker of claim 25, wherein the chemical  
moiety comprises biotin, streptavidin,  
phenylboronic acid, salicylhydroxamic acid, an  
antibody, or an antigen.

20      31. The linker of claim 25, wherein the  
dideoxynucleotide comprises a cytosine or a  
thymine with a 5-position, or an adenine or a  
guanine with a 7-position, and the linker is  
attached to the 5-position of cytosine or  
thymine or to the 7-position of adenine or  
25      guanine.

32. Use of the linker of claim 25 in DNA sequencing  
using mass spectrometry, wherein the linker  
increases mass separation between different



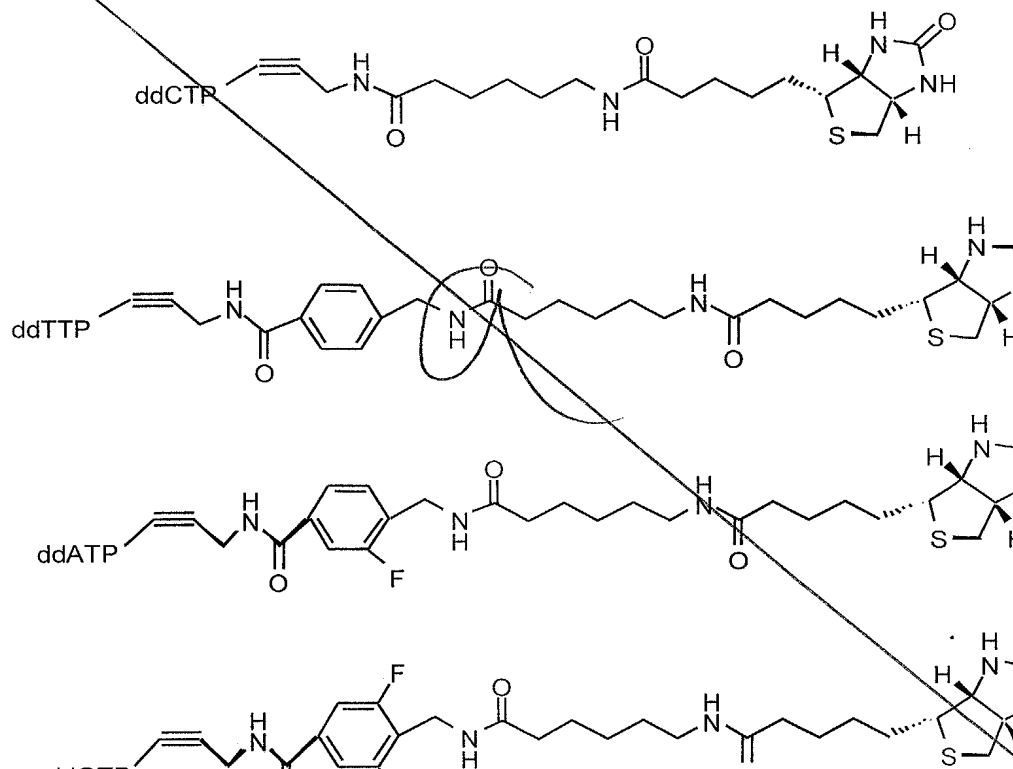
37. The labeled dideoxynucleotide of claim 33, wherein the labeled dideoxynucleotide is selected from the group consisting of:

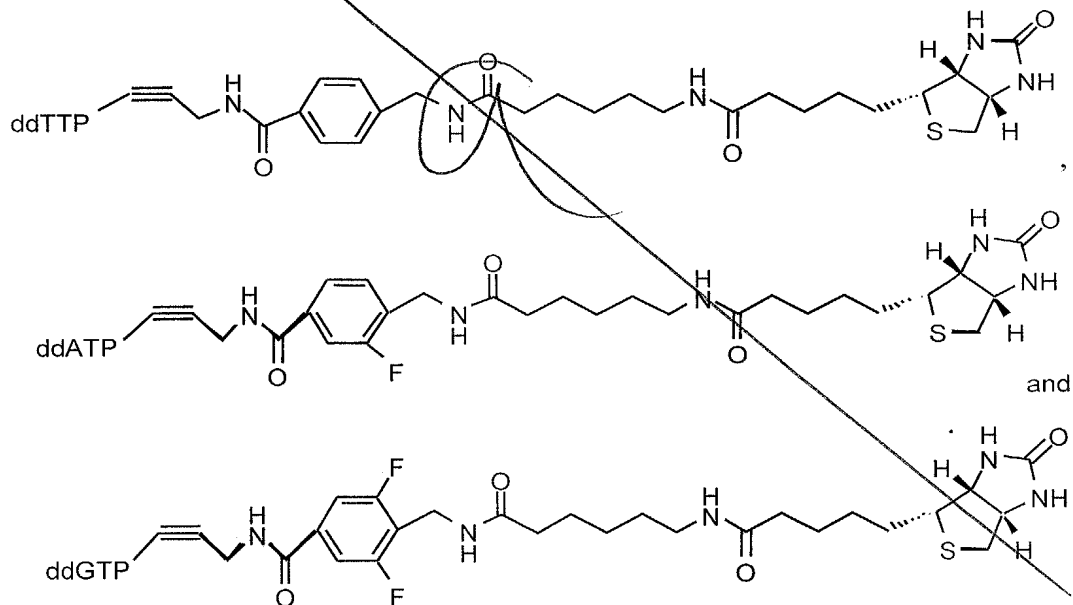


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wherein ddNTP1, ddNTP2, ddNTP3, and ddNTP4 represent four different dideoxynucleotides.

38. The labeled dideoxynucleotide of claim 37, wherein the labeled dideoxynucleotide is selected from the group consisting of:

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and

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Start of 1976	100
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End of 2099	100
End of 2100	100

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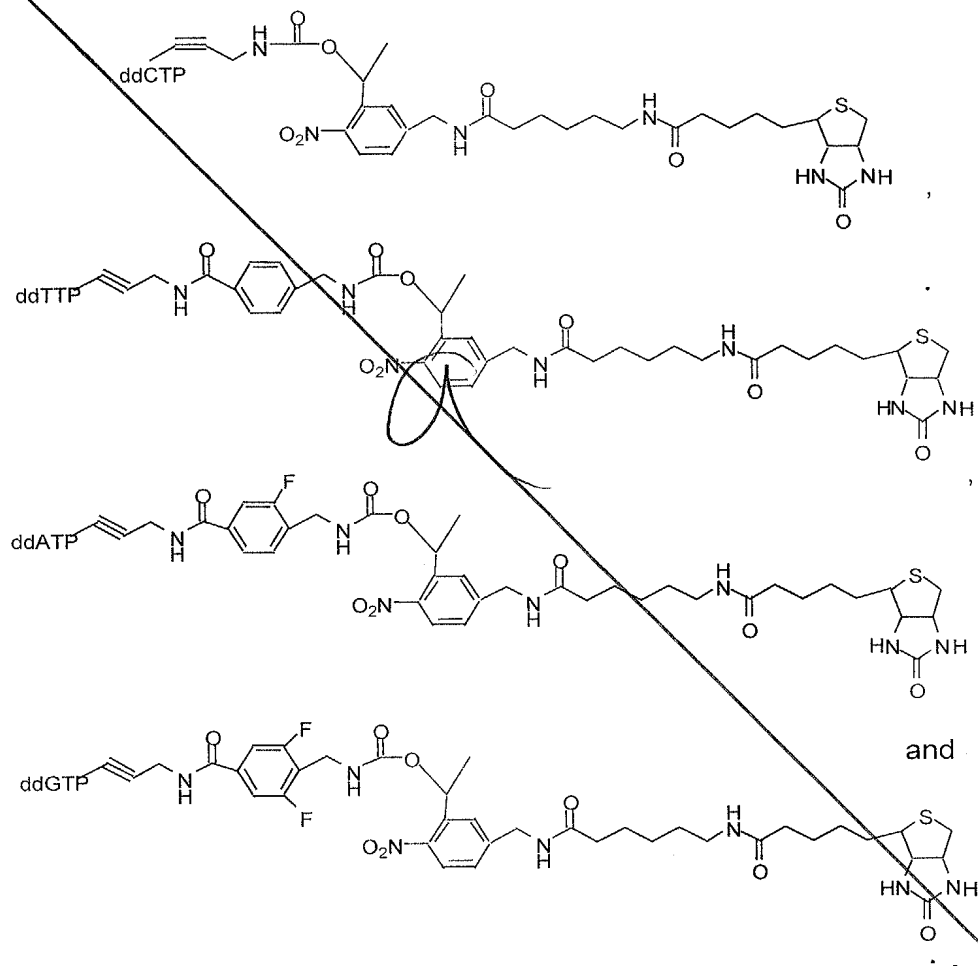


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40. The labeled dideoxynucleotide of claim 39, wherein the labeled dideoxynucleotide is selected from the group consisting of:



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41. Use of the labeled dideoxynucleotide of claim 33 in DNA sequencing using mass spectrometry, wherein the linker increases mass separation between different labeled dideoxynucleotides and increases mass spectrometry resolution.

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(d) a means for moving the sample through the channel between wells.)

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45. The system of claim 44, wherein the biotinylated moiety is a biotinylated DNA sequencing fragment.

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46. The system of claim 42, wherein the chemical moiety can be freed from the surface by disrupting the interaction between the chemical moiety and the compound coating the surface.

47. The system of claim 46, where the interaction can be disrupted by a means selected from the group consisting of one or more of a physical means, a chemical means, a physical chemical means, heat, and light.
48. The system of claim 42, wherein the chemical moiety is attached via a linker to another chemical compound.
49. The system of claim 48, wherein the other chemical compound is a DNA sequencing fragment.
50. The system of claim 48, where the linker is cleavable by a means selected from the group consisting of one or more of a physical means, a chemical means, a physical chemical means, heat, and light.
51. The system of claim 50, wherein the channel is transparent to ultraviolet light and the linker is cleavable by ultraviolet light.
52. A multi-channel system, which comprises a plurality of the system of claim 42.
53. The multi-channel system of claim 52, wherein the channels are in a chip.
54. The multi-channel system of claim 53, which comprises 96 channels in a chip.

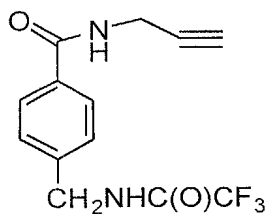
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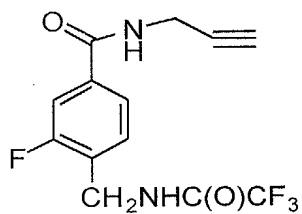
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58. The method of claim 57, wherein one or more of the different linkers is selected from the group consisting of:

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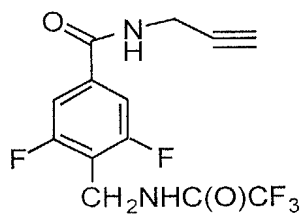


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